

Remarks

Claims 95-138 are pending in the subject application. By this Amendment, Applicants have canceled claims 105 and 132 and amended claims 95, 97, 100, 104, 106-108, 111, 114, 118-122, 124, 127, 131, 133, 134, and 135. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 95-104, 106-131 and 133-138 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claim 97 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, dependent claim 97 is worded as “further comprising a molecule...” while the independent claim 95 is drawn to “an isolated peptide consisting of”. In this regard, it is noted that independent claim 95 has been amended to recite a “conjugate or derivative of a), b), c), d), e) or f)” and claim 97 corresponds to elements that can be conjugated to the peptides recited in a), b), c), d), e) or f) of claim 95. Accordingly, reconsideration and withdrawal of the objection is respectfully requested as claim 97 further limits claim 95.

Claims 95-97, 100, 104, 106, 107, 109, 110, 111, 113-114, 120, 121, 123, 124, 126-127, 133, 134, 136, and 138 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Office Action indicates that the words “said polypeptide” are unclear in claims 95, 111 and 124, the phrase “wherein said polypeptide consists of between 5 and 10 contiguous amino acids of between 5 and 10 contiguous amino acids of SEQ ID NO: 1” is unclear in claims 100, 114, and 127, and the phrase “fused to a peptide consisting of amino acids 94-124 of human OX40L” is indefinite in claim 104. Applicants have amended the claims in an effort to attend to these issues and request the courtesy of an interview to discuss any additional issues the Examiner may identify when considering these amendments. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claim 138 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed

invention. The Office Action indicates that the specification does not disclose that the peptide is PEGylated. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention. For example, page 16, lines 5-10 of the as-filed specification clearly discusses conjugates or complexes of the claimed peptides, including conjugates containing polyethylene glycol. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 95-97, 99-100, 102-104, 106-111, 113-114, 116-118, 120-124, 126-127, 129-130 and 133 -138 are rejected under 35 U.S.C. 112, first paragraph, as nonenabled by the subject specification. The Office Action indicates that the specification is enabled for isolated peptides, compositions containing them, comprising SEQ ID NOs: 6 and 8 but is not enabled for SEQ ID NO: 13. Applicants respectfully assert that the claims as filed are enabled.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention (*Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983)) and is not precluded even if some experimentation is necessary. *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984); *W.L. Gore and Associates v. Garlock, Inc.*, 721 F.2d 1540, 1556, 220 U.S.P.Q. 303, 315 (Fed. Cir. 1983). Applicants also submit that nothing more than objective enablement is required, and therefore, it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. Additionally, the Patent and Trademark Office Board of Patent Appeals and Interferences has stated: “The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed”. *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982); *see also Ex parte Erlich* 3 U.S.P.Q.2d 1011 (B.P.A.I. 1982) (observing that although a method might be “tedious and laborious,” such experimentation is nevertheless “routine” defining “routine” experiments as those which use known methods in combination with the variables taught in the patent to achieve the expected, specific, patented result).

In this case, the as-filed specification provides adequate teaching with respect to screening assays (see, for example, pages 25-26 and Examples 1-2). The as-filed specification also provides the peptide to be tested in such assays. While testing the claimed peptide for its ability to bind to the OX40R may be laborious and/or tedious, such experimentation would not constitute undue experimentation since one was using known methods and a disclosed peptide to ascertain its ability to bind OX40R. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 95-136 are rejected under 35 U.S.C. § 103(a) as obvious over Godfrey *et al.* (U.S. Patent No. 6,242,566) in view of Chien *et al.* (1991) and Hamaoui *et al.* (1990). The Office Action indicates that Godfrey *et al.* teach purified ACT-4-L ligand polypeptides, an exemplified ACT-4-L ligand designated ACT-4-L-h-1. Chien *et al.* is cited as teaching a method by which a protein-protein interaction is identified in vivo through reconstitution of the activity of a transcriptional activator. Applicants respectfully assert that the claimed invention is not obvious over the cited references and note that the Office Action of January 22, 2009 indicates that the previously submitted arguments have been carefully considered but not found persuasive since the two-hybrid system of Chien *et al.* would have easily identified a binding motif.

Applicants submit that the current rejection is based upon improper hindsight reconstruction of the claimed invention. While Applicants recognize that such a reconstruction of the invention is proper so long as an obviousness rejection takes into account only the knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicants' disclosure (*In re McLaughlin*, 443 F.2d 1392, 1395, 170 U.S.P.Q. 209, 212 (C.C.P.A. 1971)), it is respectfully submitted that Applicants' disclosure has been used to serve as the basis of the rejection currently of record.

Applicants submit that the current finding of obviousness for the claimed invention is based upon the impermissible use of the data and knowledge gleaned from the as-filed specification. As noted previously, the as-filed specification indicates (at page 2) that:

OX40L interacts with OX40R as a homotrimer with a high affinity ( $K_d = 0.2$ - $0.4$  nM), and various binding assays have been tested on this system (Taylor L et al, 2002; Taylor L and Schwartz H, 2001; Al-Shamkhani A et al., 1997). However, no tridimensional structure has been solved so far, neither detailed structure-activity

studies have been performed, in order to provide any further molecular details on the mechanism of OX40L-OX40R interaction.

Thus, the as-filed specification indicates that it is unknown whether OX40L interacts with its cognate receptor via a linear peptide or via a conformational arrangement of the homotrimer and the cited combination of references provides no teaching as to why one of skill in the art, in view of such a recognition, would, **absent the teachings of the as-filed specification**, have had a reasonable expectation of identifying linear peptides having the ability to bind to OX40R and antagonize its activity.

Applicants further note that only large molecules, such as the extracellular domain of OX40L or antibodies that bind to OX40R, were recognized in the art as being effective OX40R binding agents (see paragraph bridging pages 3-4 of the as-filed specification) and that the majority of these agents were recognized to be agonists of OX40R. Thus, **absent the teachings of the as-filed specification**, one skilled in the art would not have expected small linear peptides would have had the ability to bind to OX40R and antagonize the activity of the receptor and/or its interaction with OX40L. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claim 137 is rejected under 35 U.S.C. § 103(a) as obvious over Godfrey *et al.* (U.S. Patent No. 6,242,566) in view of Chien *et al.* (1991) and Hruby *et al.* (2000). The Office Action states that Hruby *et al.* teach the design of peptidomimetic ligands with agonist biological activities. Applicants respectfully assert that the claimed invention is not obvious over the cited references and that the addition of Hruby *et al.* does nothing to cure the issues noted above with respect to the combined teachings of Godfrey *et al.* and Chien *et al.* Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Claim 138 is rejected under 35 U.S.C. § 103(a) as obvious over Godfrey *et al.* (U.S. Patent No. 6,242,566) in view of Chien *et al.* (1991) and Quillan *et al.* (U.S. Patent No. 6,602,856). The Office Action notes that Quillan *et al.* teach peptide antagonists of  $\alpha$ -melanocyte stimulating hormone. Applicants respectfully assert that the claimed invention is not obvious over the cited references and that the addition of Quillan *et al.* does nothing to cure the issues noted above with

respect to the combined teachings of Godfrey *et al.* and Chien *et al.* Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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